TSHR gene

thyroid stimulating hormone receptor

Normal Function

The *TSHR* gene provides instructions for making a protein, known as a receptor, that attaches (binds) to a hormone called thyroid stimulating hormone (TSH). This receptor spans the membrane of certain cells (called follicular cells) in the thyroid gland, a butterfly-shaped tissue in the lower neck. A large part of the receptor sits on the outer surface of the cell (extracellular), and a small portion is retained inside the cell (intracellular). Thyroid stimulating hormone binds to the extracellular portion of the receptor like a key fitting into a lock, activating a series of reactions that control development of the thyroid gland and its functions. Among its functions, the thyroid gland produces iodine-containing hormones (thyroid hormones), which help regulate growth, brain development, and the rate of chemical reactions in the body (metabolism).

Health Conditions Related to Genetic Changes

congenital hypothyroidism

Several *TSHR* gene mutations have been identified in people with congenital hypothyroidism, a condition characterized by abnormally low levels of thyroid hormones starting from birth. *TSHR* gene mutations change one of the protein building blocks (amino acids) used to make the thyroid stimulating hormone receptor. Some of these mutations prevent the receptor from properly spanning the membrane, and in some cases the entire receptor is retained inside the cell. As a result, the receptor cannot interact properly with thyroid stimulating hormone. Other mutations impair the receptor's ability to bind with thyroid stimulating hormone, even though the receptor correctly spans the membrane.

Without properly functioning receptors, thyroid hormone production is not stimulated. The body tries to correct the blocked stimulation by producing more thyroid stimulating hormone. In some cases, the increased levels of thyroid stimulating hormone compensate for receptors with minor defects, and the thyroid functions normally. In other cases, thyroid hormone levels remain low, causing mild to severe congenital hypothyroidism. Impaired thyroid stimulating hormone receptors may also disrupt thyroid development, and as a result, the gland is smaller than normal. Cases of congenital hypothyroidism caused by *TSHR* gene mutations are sometimes classified as thyroid dysgenesis because development of the thyroid gland is impaired.

Graves disease

tumors

Sometimes gene mutations are acquired during a person's lifetime and are present only in certain cells. This type of mutation is called somatic, and it is not inherited. Somatic mutations in the *TSHR* gene have been identified in thyroid tumors. These mutations are found only in the tumor cells.

Somatic *TSHR* gene mutations have been reported in many cases of noncancerous (benign) thyroid tumors, called nodules or adenomas, which are associated with an overactive thyroid (hyperthyroidism). Somatic mutations have also been identified in some cancerous (malignant) thyroid tumors known as thyroid carcinomas. As a result of these somatic mutations, the thyroid stimulating hormone receptor is continuously activated, which could prompt the overgrowth of thyroid cells.

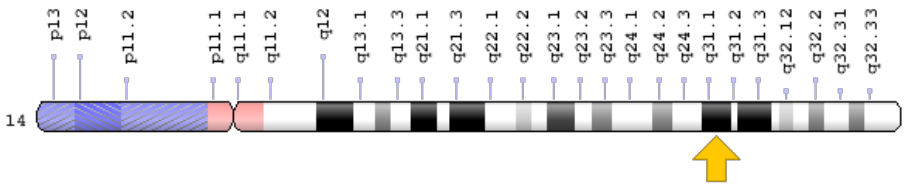
other disorders

TSHR gene mutations can cause disorders associated with hyperthyroidism. These mutations change one of the amino acids used to make the thyroid stimulating hormone receptor. As a result, the receptor is continuously activated and overstimulates the production of thyroid hormones. *TSHR* gene mutations can lead to an enlarged thyroid gland (goiter) and symptoms of hyperthyroidism, such as a rapid heartbeat. Hyperthyroidism that is present from birth is called nonautoimmune congenital hyperthyroidism (or sporadic toxic thyroid hyperplasia). Onset of hyperthyroidism that begins in childhood or adulthood is known as nonautoimmune autosomal dominant hyperthyroidism (or hereditary toxic thyroid hyperplasia).

Chromosomal Location

Cytogenetic Location: 14q31.1, which is the long (q) arm of chromosome 14 at position 31.1

Molecular Location: base pairs 80,954,989 to 81,146,302 on chromosome 14 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- LGR3
- thyrotropin receptor
- TSH Receptors
- TSHR_HUMAN

Additional Information & Resources

Educational Resources

- The New York Thyroid Center
  http://columbiasurgery.org/node/992

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28TSHR%5BTIAB%5D%29+OR+%28thyroid+stimulating+hormone+receptor%5BTIAB%5D%29%29+AND+%28%28receptors,+thyroid+stimulating+hormone%5BMH%5D%29+OR+%28tsh+receptors%5BMH%5D%29+OR+%28thyrotropin+receptor%5BMH%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- HYPERTHYROIDISM, NONAUTOIMMUNE
  http://omim.org/entry/609152
- THYROID-STIMULATING HORMONE RECEPTOR
  http://omim.org/entry/603372

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/TSHRID290ch14q31.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=TSHR%5Bgene%5D
- HGNC Gene Family: Glycoprotein hormone receptors
  http://www.genenames.org/cgi-bin/genefamilies/set/199
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=12373

- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/7253
- UniProt
  http://www.uniprot.org/uniprot/P16473

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